PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No. 01-1081)

In the Application of:	)	
	)	
Graf *et al.*	)	**Examiner: Ford, Vanessa L.**
	)	
Application No.: 09/937,103	)	**Group Art Unit: 1645**
	)	
Filing Date: July 5, 2002	)	**Confirmation No.: 4719**
	)	
For: Use of Trehalose For Stabilizing A Liquid Vaccine	)	

PRE-APPEAL BRIEF REVIEW REQUEST
PURSUANT TO OG NOTICE OF 12 JULY 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The applicants request pre-appeal brief review of the pending rejections. This paper sets forth applicants' concise statement of clear errors in the Examiner's rejections. By separate paper filed concurrently, claims 2-8, 11-15, and 17 have been canceled to narrow the issues for review. Applicants do not acquiesce to the rejections, however, and retain the right to pursue the canceled claims and subject matter in a continuing application.

With cancellation of claims 2-8, 11-15, and 17, there is only a single rejection remaining. This is the rejection of claims 9-10 and 16 under 35 U.S.C. § 103(a) as obvious over Samaritani in view of Sola-Penna *et al.* and further in view of Anderson *et al.*

First, there is no suggestion or motivation in the cited art to make the presently claimed invention. Samaritani teaches the use of a non-reducing sugar generally and sucrose specifically to enhance the stability of the protein hCG (human Chorionic Gonadotropin) and liquid formulations thereof to maintain the hormonal activity of hCG.[1] Samaritani does not provide any teachings or suggestions

[1] In their last response, the applicants mistakenly asserted that Samaritani teaches the use trehalose for stabilizing hCG. Samaritani does not mention trehalose at all.

regarding the use of a non-reducing sugar for the stabilization of any other macromolecule. Samaritani is not concerned with, nor does it consider, the immunogenicity of hCG. More generally, Samaritani does not contemplate the use of a non-reducing sugar to maintain the immunogenicity of an antigen, generally, or a polysaccharide conjugated to a carrier protein, in particular. Samaritani is completely silent as to the effects of a non-reducing sugar on the immunogenicity of an antigen. This is not surprising as Samaritani is concerned not with immunogenicity at all but, as noted above, with maintaining the hormonal activity of hCG, only.

Sola-Penna *et al.* provides a study of trehalose as a stabilizer of "macromolecules," but the only macromolecules considered are enzymes and the stabilization studied was with respect to thermal effects on enzymatic activity. Sola-Penna, like Samaritani, is not concerned with immunogenicity. Consequently, there is no teaching or suggestion in Sola-Penna *et al.* that trehalose would stabilize immunogenicity of an antigen.

Anderson *et al.* provides no teachings regarding stabilization of the disclosed polysaccharide-protein carrier conjugates.

In brief, none of the cited art, alone or in combination teach or suggest the particular combination of trehalose with a polysaccharide-protein conjugate antigen. None recognize that trehalose can decrease the decay of immunogenicity of a polysaccharide-protein conjugate in a liquid vaccine composition. Samaritani and Sola-Penna *et al.* are concerned with stabilizing enzymatic activity. But a polysaccharide-protein conjugate for use in liquid vaccine compositions has no such activities and is not employed for that purpose. Accordingly, any motivation supplied by Samaritani and Sola-Penna *et al.* to stabilize enzymatic activity would not motivate one to combine trehalose with a polysaccharide-protein conjugates in liquid vaccine compositions. Therefore, none of Samaritani, Sola-Penna *et al.*, or Anderson, alone or in combination, can provide a suggestion or motivation to combine trehalose with a polysaccharide-protein conjugate. Indeed, as the components of a liquid vaccine composition are not relied upon for their enzymatic activity, the motivation to use a non-reducing sugar like trehalose to stabilize enzymatic activity simply does not apply to a liquid vaccine composition.

Furthermore, without supplying a teaching or even recognition that trehalose can stabilize the immunogenicity of a polysaccharide-protein conjugate antigen, the cited art could not have imbued the ordinary artisan with a reasonable expectation that adding trehalose to a polysaccharide-protein

conjugate containing liquid vaccine composition would enhance the immunogenic stability of the polysaccharide-protein conjugate. Indeed, given that the components of liquid vaccine compositions are not relied on for enzymatic activity, none of the cited art provides any teachings that adding trehalose to a liquid vaccine composition would have any affect at all on such a composition.

For these reasons claims 9-10 and 16 cannot be obvious over the cited art. Accordingly, the applicants respectfully request reconsideration and withdrawal of this § 103 rejection.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of the pending § 102 and § 103 rejections. If there are any questions or comments regarding this response or application, the Office is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

Date: February 24, 2006

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